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Mr. Chairman, and members of the Committee, I am pleased to be here on behalf of the National Institute of Mental Health (NIMH) to tell you about our great progress in understanding the biological basis of mental illnesses, and about our active collaborations with our fellow research institutes, the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and with the Substance Abuse and Mental Health Services Administration (SAMHSA). The FY 2006 budget includes $1,417,692,000, which reflects an increase of $5,759,000 over the 2005 enacted level of $1,411,933,000 comparable for transfers proposed in the President's request. In my statement, I will call to your attention our Nation's immense burden of mental and behavioral disorders, provide a brief review of our research activities and accomplishments, and describe some of our ongoing collaborations with NIDA, NIAAA, and SAMHSA.

BURDEN OF MENTAL ILLNESS

The mission of the NIMH is to reduce the public health burden of mental and behavioral disorders. New scientific discoveries and powerful new tools are revealing the mechanisms involved in the pathophysiology of mental disorders. This is a vital step in the development of more effective strategies to manage, treat, and even prevent these debilitating disorders.

The report of the President's New Freedom Commission: Achieving the Promise--Transforming Mental Health Care in America defined the challenge. The burden of these disorders is staggering, in terms of both morbidity and mortality. Mental illness and substance abuse represent the top 5 sources of disability caused by noncommunicable diseases for ages 15-44 in the United States and Canada, according to

the World Health Organization. Suicide accounts for more deaths each year than either homicide or AIDS. Of the 30, 000 Americans who die by suicide each year, 90 percent have a mental illness.

Mental and substance abuse disorders are inherently intertwined, with co-occurring (comorbid) diagnoses of substance abuse and mental disorders affecting as many as 7-10 million people in the United States. Substance use disorders are especially prevalent in individuals with schizophrenia (47%), bipolar disorder (45%), anxiety (25%), and major depression (24%), exhibited through abuse or dependence of either alcohol or drugs.

In addition to the emotional costs, the economic costs of mental illness are striking. According to the Commission's report, the costs of treating mental disorders are estimated at $150 billion per year, with elements of these expenses rapidly increasing beyond 20 percent annually. Based on a separate analysis, in 2000, the estimated total cost of depression alone was $83.1 billion. Direct, treatment-related costs for depression were approximated at $26.1 billion, while the indirect costs due to lost workdays and reduced productivity amounted to $57 billion.

Unlike many other medical disorders, the indirect costs for mental illnesses are greater than the direct costs. Individuals with serious mental illnesses represent the single largest diagnostic group (35%) on the Supplemental Security Income payrolls. More than 50% of all mental health expenditures are paid for by the public sector, including Medicaid, Medicare, and state and local government. Medicaid is the largest single payer of mental health services in the country. Presented with these great health

and economic challenges, NIMH is working closely with SAMHSA to transform mental health care with the ultimate goal of patient recovery.

MENTAL DISORDERS ARE BRAIN DISORDERS

A major goal for NIMH is to identify the biological basis of mental disorders to more precisely pinpoint targets for prevention and treatment. This means understanding the neural basis of the illness at all levels, from molecular to behavioral. New findings resulting from the *NIMH Human Genetics Initiative* and several brain imaging studies have demonstrated that mental disorders have a biological basis.

Several genes have been implicated in the susceptibility to schizophrenia and depression. In the past year, we have learned that subtle genetic variations bias the way the brain works, and may increase vulnerability to mental illness. For instance, a gene variant associated with schizophrenia appears to increase the amount of activity in the frontal lobe needed to perform complex attentional tasks. Studies of people with major depressive disorder reveal that standard antidepressant medication may be less helpful in those with specific genetic variations, but these patients may respond well to cognitive behavior therapy.

In addition to studies at the molecular level, imaging tools provide a window into the inner workings of the entire brain. For instance, imaging studies reveal that for people with major depressive disorder, those with specific patterns of brain activation may be resistant to standard antidepressant medications. In another NIMH study of people with panic disorder, brain scans show that a type of receptor for serotonin (a mood-regulating neurotransmitter) is reduced by nearly a third in several structures of the brain that mediate anxiety. The finding is the first in living humans to show that this

specific receptor, which is pivotal to the action of anti-anxiety medications, may be abnormal in this disorder.

Autism continues to be a top priority for NIH. We are just beginning to see the pay-offs of cross-Institute investments in several new centers and projects. For example, recent findings indicate that the fundamental pathology may be "miswiring" in the brains of autistic children, with an excess of local circuits and a deficit of long-range circuits. Furthermore, studies show that on average, autism is not diagnosed in children until after the age of five, a relatively late age considering that early intervention is critical for the best treatment response. Thus, NIMH research is helping to develop new tools for detecting autism early, before age two. In a new study on infant siblings of children with autism, early findings indicate that siblings later diagnosed with autism show social deficits, visual attention impairments, and unusual temperament by 12 months of age. This work could greatly enhance efforts for early detection and treatment.

EVIDENCE-BASED TREATMENTS FOR RECOVERY AND DISSEMINATION

The first of several large, NIMH-funded clinical studies testing various treatment options for those with serious mental illnesses was completed last summer: a 13-site trial aimed at defining the most effective and safe treatment for children and adolescents with major depressive disorder. Depression is an important risk factor for suicide, the third leading cause of death among adolescents; it is also a major risk factor for long-term psychosocial impairment in adulthood. There has been much debate about whether a class of antidepressant medications, selective serotonin re-uptake inhibitors (SSRIs) can actually increase suicidal thinking. The NIMH-funded clinical trial defined the

most effective and safe treatment for children and adolescents with major depression. Results revealed that a combination of fluoxetine (Prozac) and a type of psychotherapy called cognitive behavioral therapy (CBT) was the most effective treatment (71% responded). Suicidal thinking, which was present in 29% of the participants at the beginning of the study, improved significantly in all four treatment groups, with those receiving medication and therapy showing the greatest reduction. Soon we will know the effectiveness of these treatments over a six-month period from treatment initiation. It is critical for physicians and psychotherapists to closely monitor their young patients on antidepressant medications for signs of hurtful or suicidal behavior, particularly during the early phases of treatment.

A central focus of NIMH treatment research has been finding a more tailored, individual approach to therapy. To personalize treatments, we need to know predictors of treatment response. Recent studies have begun to reveal some predictors that will help clinicians optimize care. For instance, studies of people with major depressive disorder reveal that standard antidepressant medication may be less helpful in those with a history of trauma, or specific genetic variations, or specific patterns of brain activation as seen on imaging scans. These same patients may respond well to cognitive behavior therapy. Similarly, patients with schizophrenia who have poor attentional processing and other cognitive deficits may report less satisfaction with anti-psychotic medications, which were not designed to treat these features of the illness. Ongoing research seeks to find markers that will guide individual treatment to optimize recovery.

Other large trials to be completed within the next year will answer urgent questions about the choice of treatments in people with bipolar disorder, schizophrenia

and Alzheimer's, and treatment-resistant major depression. NIMH continues its strong commitment to public dissemination of findings from these clinical trials by fostering partnerships with national and state organizations via the Outreach Partnership Program. Through this program, NIMH works with the National Institute on Drug Abuse and SAMHSA to bridge the gap between research and clinical practice.

SCIENCE TO SERVICE

For many mental disorders, there is some form of treatment, but there is no cure. The report from the President's New Freedom Commission on Mental Health describes the need for transforming care systems to enable better delivery of evidence-based practices and programs to communities where they can directly benefit people with mental illnesses. To achieve this goal, NIMH partners with other institutes and organizations, including NIDA, NIAAA, SAMHSA, state governments, and advocacy groups, to work toward rapid and effective distribution and implementation of science-based information about mental disorders, substance abuse, and co-morbidity.

In one such example, NIMH and SAMHSA have funded nine one-year grants to state mental health agencies to plan service and science agendas related to the implementation of evidence-based practices. Proposed science-to-service research activities include development of measures to assess the fit of specific evidence-based practices to local mental health service settings; determining relevant evidence-based practices for specific ages, such as children and adults; managing medication for those with schizophrenia; and providing cognitive behavioral therapy for people with depression. Each grant is expected to result in future research and service development initiatives, so that questions relevant to statewide implementation of effective treatments

are reflected in NIMH's services research portfolio. Translating scientific breakthroughs into far-ranging clinical care, we believe, is best achieved through a partnership between families, practitioners, and state level representatives.

BLUEPRINT FOR NEUROSCIENCE RESEARCH

The NIH Blueprint for Neuroscience is a framework to enhance cooperation among the 15 NIH Institutes and Centers that have common interests in the nervous system, including NIMH, NIDA, and NIAAA. By pooling resources and expertise, the Institutes and Centers can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community. The Blueprint is developing a primary set of initiatives including a gateway to existing databases that permits more effective searches; training enhancement for basic neuroscientists; and expansion of ongoing pediatric imaging, gene microarray, and gene expression database efforts.

NIH ROADMAP

NIMH has assumed a lead role on the Molecular Libraries and Imaging initiative of the NIH Roadmap, whose goal is to provide organic compounds called "small molecules" to scientists to use as tools to improve our understanding of biological pathways in health and disease. The potential of scientific discoveries of clinical relevance is enormous. The NIMH mission can be advanced by the identification of even one novel small molecule with biological activity in the brain, as it could provide invaluable information about brain circuits involved in mental illness and those that are altered by treatment. Collaborations such as this across NIH and with other government

agencies will provide the synergy needed to create potent strategies for recovery and prevention from mental disorders.

Thomas R. Insel, M.D.
Director, National Institute of Mental Health

Thomas R. Insel, M.D., is Director of the National Institute of Mental Health (NIMH), the component of the National Institutes of Health charged with generating the knowledge needed to understand, treat, and prevent mental disorders. With a budget of over $1.3 billion, the NIMH leads the nation's research on disorders that affect an estimated 44 million Americans, including one in five children.
Immediately prior to his appointment as Director, which marks his return to NIMH after an 8-year hiatus, Dr. Insel was Professor of Psychiatry at Emory University. There, he was founding director of the Center for Behavioral Neuroscience, one of the largest science and technology centers funded by the National Science Foundation and, concurrently, director of an NIH-funded Center for Autism Research. From 1994 to 1999, he was Director of the Yerkes Regional Primate Research Center in Atlanta. While at Emory, Dr. Insel continued the line of research he had initiated at NIMH studying the neurobiology of complex social behaviors in animals. A particular focus of his work has examined the role of the neuropeptides oxytocin and vasopressin in social attachment – including, for example, maternal behavior and pair-bond formation – and in aggressive behavior. This work established his place on the ISI's list of the 200 most frequently cited neuroscientists in the 1990s. Early in his NIMH research career, which extended from 1979 to 1994, Dr. Insel conducted clinical research on obsessive-compulsive disorder, conducting some of the first treatment trials for OCD using the selective serotonin reuptake inhibitors (SSRI) class of medications. He has published over 200 scientific articles and four books, including the Neurobiology of Parental Care (with Michael Numan) in 2003.

Dr. Insel has served on numerous academic, scientific, and professional committees, including 10 editorial boards. He is a member of the Institute of Medicine, a fellow of the American College of Neuropsychopharmacology, and is a recipient of several awards [A. E. Bennett Award from the Society for Biological Psychiatry, Curt Richter Prize from the International Society of Psychoneuroendocrinology, Outstanding Service Award from the U.S. Public Health Service, and a Distinguished Investigator Award from the National Alliance for Research on Schizophrenia and Depression (NARSAD)].
Dr. Insel graduated from the combined B.A.-M.D. program at Boston University in 1974. He did his internship at Berkshire Medical Center, Pittsfield, Massachusetts, and his residency at the Langley Porter Neuropsychiatric Institute at the University of California, San Francisco.

Department of Health and Human Services
Office of Budget
William R. Beldon

Mr. Beldon is currently serving as Deputy Assistant Secretary for Budget, HHS. He has been a Division Director in the Budget Office for 16 years, most recently as Director of the Division of Discretionary Programs. Mr. Beldon started in federal service as an auditor in the Health, Education and Welfare Financial Management Intern program. Over the course of 30 years in the Budget Office, Mr. Beldon has held Program Analyst, Branch Chief and Division Director positions. Mr. Beldon received a Bachelor's Degree in History and Political Science from Marshall University and attended the University of Pittsburgh where he studied Public Administration. He resides in Fort Washington, Maryland.